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09/744,751	06/01/2001	Seo Young Jeong	GRT/912-25	4257
23117 7590 07/10/2007 NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203				
EXAMINER SULLIVAN, DANIEL M				
ART UNIT		PAPER NUMBER		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/744,751

Applicant(s)

JEONG ET AL.

Examiner

Daniel M. Sullivan

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30 and 44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 30 and 44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is a reply to the Paper filed 12 June 2007 in response to the Final Office Action mailed 12 March 2007. Finality of the previous Office Action is withdrawn in view of the new grounds for rejection set forth herein below.

Claims 1, 3, 5-13, 22-27, 29, 30, 40, 42 and 44 were considered in the 12 March Office Action. Claims 1, 3, 5-13, 22-27, 29, 40 and 42 were cancelled in the 12 June Paper. Claims 30 and 44 are pending and under consideration.

Response to Amendment and Arguments

The claim rejections set forth in the previous Office Action are rendered moot by the cancellation of the rejected claims.

New Grounds for Objection/Rejection

Claim Objections

Claim 30 is objected to because of the following informalities: Although the instant claims construed in light of the supporting disclosure are clearly directed to oil-in-water emulsions comprising both a non-triglyceride oil and a cationic transfection agent, claim 30, as written, could be viewed as reading on an oil-in-water emulsion comprising any one of the recited components because the only conjunction used is "or". The following amendment is suggested to clarify that the oil-in-water emulsion must comprise both a non-triglyceride oil and one or more cationic lipid transfection agents.

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30. (Currently amended) A complex of an oil-in-water emulsion for delivering DNA, RNA, antisense nucleic acid, polynucleotide, or oligonucleotide; wherein said emulsion comprises: an oil phase comprising 2-30% of non-triglyceride oil, 0.01 -20% of one or more cationic lipid transfection agents, and further comprising taxol, paclitaxel or fluorouracil-in oil phase; and water to 100%.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sankaram et al. US Patent No. 5,766,627 in view of Liu et al. (1997) WO 97/11682 (previously made of record).

The instant claim 30 is directed to complex of an oil-in-water emulsion comprising 2-30% of non-triglyceride oil, 0.01-20% of one or more cationic lipid transfection agents, taxol, paclitaxel or fluorouracil in oil phase, and water to 100%.

Sankaram et al. claims a process for a producing a liposome comprising a forming a water-in-oil emulsion comprising a lipid component comprising at least one amphipathic lipid, at least one neutral lipid lacking a hydrophobic head group, and a first aqueous component, wherein the emulsion further comprises at least one biologically active substance that could be an antitumor agent. (See especially claim 1.) In claim 19, Sankaram et al. contemplates embodiments wherein the composition comprises diacyl trimethylammonium propanes or diacyl dimethylammonium propanes (i.e., cationic lipid transfection agents) in the amphipathic lipid portion and in claim 20 Sankaram et al. contemplates embodiments wherein the neutral lipid is a non-triglyceride oil, including squalene. Sankaram et al. further teaches that 5-fluorouracil is among the anticancer agents that might be comprised by the emulsion. (See especially column 5, line 32.)

Thus, Sankaram et al. teaches a method of producing an oil-in-water emulsion wherein the teachings include an embodiment wherein the oil-in-water emulsion comprises a cationic lipid transfection agent, a non-triglyceride oil and fluorouracil. Sankaram et al. does not teach that the lipid components should be provided at the concentrations recited in the claims.

Liu et al. also teaches an oil-in-water lipid emulsion for delivering biologically active material comprising a total lipid component of from about 0.001 to about 20% with the remainder being aqueous carrier. (See especially p. 7, ¶ 2.) Liu et al. further teaches, of the total lipid, the amphiphile is preferably present in an amount from about 5 to about 80 weight % (p. 7,

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¶3) and the oil component is present in an amount from about 10 to about 80 weight % of the total lipid components. Thus, in the composition of Liu et al., the amphiphile is present at approximately 0.0005% to approximately 16% of the total composition and the oil is present in an amount from about 0.0001 to about 16% of the total composition. Liu et al. further teaches that the oil component can be diethylglycerol (a non-triglyceride oil; see especially p. 10, l. 3) and that the amphiphile can be selected from any one of several cationic lipid transfection agents (e.g., N-[1-(1,2-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride; p. 10, ll. 15-16).

Thus, Liu et al. teaches an oil-in-water lipid emulsion comprising a non-triglyceride oil and a cationic lipid transfection agent, wherein the range of oil and cationic lipid concentrations contemplated by Liu et al. overlap with the ranges recited in the instant claims.

The teachings of Sankaram et al. and Liu et al., considered as a whole, demonstrate that it was known in the art at the time the instant application was filed to produce oil-in-water emulsions comprising of non-triglyceride oil and one or more cationic lipid transfection agents. Sankaram et al. teaches that these emulsions can be used to deliver anticancer agents such as fluorouracil and Liu et al. teaches the inclusion of non-triglyceride oil and cationic lipid transfection agents in concentrations that overlap with the ranges recited in the claims. In view of this, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Sankaram et al. and Liu et al. according to the limitations of the instant claims. Liu et al. teaches non-triglyceride oil and cationic lipid concentration that can be used to produce oil-in-water emulsions capable of delivering biologically active substances. One would be motivated to use the non-triglyceride oil and

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cationic lipid concentrations taught by Liu et al. in practicing the method of Sankaram et al. because they are recognized in the art as effective.

Absent evidence to the contrary, one would have a reasonable expectation of success in combining the teachings of the prior art because the art evidences that production of oil-in-water emulsions using non-triglyceride oil and cationic lipids was routine in the art at the time the instant application was filed.

In view of the foregoing, the claimed invention, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC § 103(a) as obvious over the art.

Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sankaram et al. US Patent No. 5,766,627 in view of Liu et al. (1997) WO 97/11682 (previously made of record) and further in view of Goodman and Gilman's The Pharmacological Basis of Therapeutics, 8th edition, (Goodman Gilman, Rall, Nies and Taylor, eds.), Pergamon Press, Inc., NY, 1990, pp. 1267-1270 (hereinafter, Goodman and Gilman).

The instant claim 44 is directed to complex of an oil-in-water emulsion comprising 2-30% of non-triglyceride oil, 0.01-20% of one or more cationic lipid transfection agents, and cyclosporin in oil phase, and water to 100%.

As described above, the teachings of Sankaram et al. in view of Liu et al. render obvious the oil-in-water emulsion of the claims. Sankaram et al. in view of Liu et al. do not explicitly teach an embodiment wherein the emulsion comprises cyclosporine. However, Sankaram et al.

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does teach that immunomodulators are among the biologically active substances that might be comprised by the oil-in-water emulsion contemplated therein. (See especially claim 1.)

Goodman and Gilman teaches, "The introduction of cyclosporine has provide an entirely new approach to immunosuppression by virtue of its highly selective ability to inhibit activation of T cells []. Unlike cytotoxic immunosuppresants, therapeutic concentrations of cyclosporine do not cause myelosuppression." (Paragraph bridging pages 1267-1268.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include cyclosporine among the immunomodulators comprised by the oil-in-water emulsion of Sankaram et al. One would be motivated to do so because Sankaram et al. contemplates immunomodulators as among the biologically active substances to be comprised in the emulsion and Goodman and Gilman teaches that cyclosporine A is an immunomodulator having many advantageous properties. Absent evidence to the contrary, one would have a reasonable expectation of success in combining the teachings of the prior art because there is nothing of record to suggest that cyclosporine could not be formulated in an oil-in-water emulsion.

In view of the foregoing, the claimed invention, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC § 103(a) as obvious over the art.

Conclusion

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779.

The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Daniel M Sullivan/
Primary Examiner
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